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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/620,586	07/20/2000	Steen Klysner	0459-0464P	2471

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/620,586	KLYSNER ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-23,29 and 53-64* is/are pending in the application.

4a) Of the above claim(s) *3 -15 , 18, 55, 57 and 59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 16, 19-23, 29 and 53-54, 56, 58 and 60-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 08/12/03 is acknowledged.

Claims 1-16, 18-23, 29 and 53-64 are pending.

2. The amended claims 3 –7, 9-11, 55, 57 and newly submitted claim 59 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The elected Group I (claims 1-7, 9-11,16-17,19-23, 29 and 53-56), now claims, 1, 2, 16,19-23, 29 and 53-58 and 60-64 read on a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof, or at least one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analoge has been modified so that at least one foreign T_H epitope moiety, wherein T cell epitope is Tetanus toxoid epitope is introduced without a carrier molecule, and wherein modification is substitution in SEQ ID NO:12 at amino acid from 49-69. The amended claims 3 –7, 9-10 and newly submitted claim 59 reads on a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analoge has been modified so that at least one first moiety that effects targeting, or al least one second moiety which stimulates the immune system, or at least one third moiety which optimizes presentation of the modified GDF-8 polypeptide is introduced. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits.

Accordingly, claim 3 -10, 12-15 , 18, 55, 57 and 59 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1, 2, 16, 19-23, 29 and 53-54, 56, 58 and 60-64 read on a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof, or at least one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analoge has been modified so that at least one foreign T_H epitope moiety, wherein T cell epitope is Tetanus toxoid epitope is introduced without a carrier molecule, and wherein modification is substitution in SEQ ID NO:12 at amino acid from 49-69 under consideration in the instant application.

In view of the amendment, filed 08/12/03 the following rejections remain

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 2, 16, 19-23, 29 and 53-54, 56, 58 and 60-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barker et al.(US. Pat. No. 6,369,201) in view of the known fact disclosed in the specification on page 16, lines 24-30 for the same reasons set forth in the previous Office Action, mailed 04/08/03.

Applicant's arguments, filed 08/12/03 have been fully considered, but have not been found convincing.

Applicant asserted that US Patent '201 failed to describe the specific modification described in the claims.

Applicants have traversed the primary references pointing to the differences between the claims and the disclosure in reference. Applicant is respectfully reminded that the rejection is under 35 USC103. In considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom In re Preda, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968). See MPEP 2144.01. Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA).

As was stated in the previous Office Action , US Patent '201 teaches a method for in vivo down-regulation of myostatin (GDF-8) activity, which will result in increase in muscle mass of an animal, comprising administering at least one full length myostatin polypeptide, or at least one myostatin analogue, wherein myostatin is derived from bovine and myostatin immunoconjugate comprising at least one myostatin polypeptide, linked to an immunological carrier (see Abstract and Column 4, especially lines 1-4; column 7 lines 15-22, column 9, lines

22-35, column 13, lines 1-5 in particular). It is noted that US Patent '201 teaches SEQ ID NO:2 that is 100 % identical to SEQ ID NO:12 of the instant application. US Patent '201 teaches that the term "myostatin immunogen" includes polypeptide of myostatin molecule, analogue and modification by substitution such that a substantial fraction of myostatin B cell epitopes are preserved and do not affect the ability of the analog to induces an immunological response (see column 6, lines14-65, column 7, lines 6-15, column 15 lines 1-5, and column 16, lines 42-45 in particular). US Patent '201 teaches a myostatin multimer, wherein modification includes duplication of at least one myostatin B cell epitope (see column 7, lines 23-30 and column 8, lines 45-65 in particular).
US Patent '201 teaches modification of miostation to include vaccine composition comprising the myostatin polypeptide or analogue and formulated with various adjuvants , such as aluminum adjuvant (see column 24, lines 1-20 in particular) and "immunological carriers" , such as *Tetanus toxoid* epitope, that will enhance the immunogenicity to the molecule and which facilitates breaking of autotolerance (see Column 4, line 10-15, column 9, lines 20-45 in particular). US Patent '201 teaches various method of administering myostatin-containing formulation, including parenteral route (see column 25). US Patent '201 teaches that effective dosages can be readily established by one of ordinary skill in the art through routine trials (see column 25, line 54-56 in particular). US Patent '201 further teach that in order to facilitate breaking of autotolerance to autoantigens myostatin molecule can be modified by association with *Tetanus toxoid* epitope (see column 9, lines 20-45).

US Patent '201 does not explicitly teaches that the *Tenanus toxoid* epitope is P2 or P30 epitope or the particular modification of myostatin wherein said molecule has been modified so that at least one foreign T_H epitope moiety, wherein T cell epitope is *Tetanus toxoid* epitope is introduced at amino acid from 49-69 of myostatin SEQ ID NO:12.

The Known fact disclosed that it is well know in the art various methods of modifying a peptide self-antigen in order to obtain breaking of autotolerance, including introducing into said molecule at least one foreign T cell epitope such *Tetanus toxoid* P2 and P30 epitopes. (see page 16, lines 24-30).

It would have obvious , conventional and within the skill of a person of ordinary skill in the art at the time the invention was made to identify the exact position for substitution for *Tetanus toxoid* epitope in myostatin molecule in order to facilitates breaking of autotolerance of said molecule and to apply the teaching of the known fact disclosed in the Specification on page 16, lines 24-30 to those of US Patent '201 to obtain a claimed method for in vivo down-regulation of GDF-8 comprising administering one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analogue has been modified so that at least one foreign T_H epitope moiety, wherein T cell epitope is Tetanus toxoid epitope is introduced without a carrier molecule, and wherein modification is substitution in myostatine molecule of SEQ ID NO:12 at amino acid from 49-69.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because it well know in the art that modifying a peptide self-antigen by introducing into said molecule at least one foreign T cell epitope (*Tetanus toxoid* epitope in particular) will facilitates breaking of autotolerance, as taught by the Known fact disclosed in the Specification on page 16, lines 24-30 and can be further used in the method for in vivo down-regulation of myostatin (GDF-8) activity, taught by US Patent '201.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 20, 21, 23, 60, are included because it would be conventional and within the skill of a person of ordinary skill in the art at the time the invention was made to : (i) determine an effective amount of myostatin polepeptide; or (ii) determine the optimum duration and means of administration. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Claims 29 and 63 are included because the claimed functional limitation would be an obvious properties of the referenced method in vivo down-regulation of myostatin (GDF-8) activity, which will result in increase in muscle mass of an animal, because the reference method using the same method steps and ingredients as the claimed method. It is clear that both the prior art and claimed method administer the same treatment to achieve the same results. When the prior art method is the same as a method described in the specification, it can be assumed the method will obviously perform the claimed process.

The following new ground of rejection are necessitated by the amendment filed 08/12/03

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

6. Claims 1, 2, 16, 19-23, 29 and 53-54, 56, 58 and 60-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

"... wherein said first amino acid sequence is from one or more of residues 1-12, 18-41, 43-48, 49-69, or 79-104 in SEQ ID NO;11 or 12 " claimed in Claim 1, line 13, represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from. The specification and the claims as originally field only support " wherein said first amino acid sequence is from one of residues 1-12, 18-41, 43-48, 49-69, or 79-104 in SEQ ID NO;11 or 12.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 16, 54, 56, 61, 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 16, 54, 56, 61 each recites "GDF-8 and a subsequence thereof '. There is insufficient antecedent basis for this limitation in the base claim 1.

B. Claim 64 is indefinite and ambiguous in the recitation of " ... that is modified by substituting at least one first amino acid sequence is made in SEQ ID NO:12". It is unclear what Applicant means by this phrase?

9. No claim allowed

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
October 20, 2003

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